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NEUROPATHOLOGICAL CHANGES IN THE DILATED PORTION OF THE CONGENITAL MEGACOLON

by

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I. INTRODUCTION

In 1948 WHITEHOUSE and KERNOHAN pointed out the poor development or the lack of the ganglion cells in AUERBACH's plexus at the strictured portion of congenital megacolon (HIRSCHSPRUNG's disease) as the characteristics of the disease. Later, SWENSON (1948), BODIAN (1949), HIATT (1951), and YOKOI (1953) reported the same interpretation as WHITEHOUSE did. Recently, UEDA attracted attention to his report that a decrease in the number of ganglion cells was found in AUERBACH's plexus of the dilated portion as well as the lack of them in the strictured portion. WANG (1955) reported that abnormally thick and reticulated autonomic nerves were found in the mucous membrane of the dilated portion.

The author found new neuropathological changes in the dilated portion of a congenital megacolon.

II. MATERIALS AND METHODS

A part of the removed dilated portion of a 26 year old congenital megacolon case was fixed in 10% neutralized formalin solution for 3 months. Blocks were taken from the dilated portion in the distal half of descending colon; 30~40μ thick sections were cut by the freezing method in parallel with the surface of the mucosa; the specimens were fixed in 10% formalin for more than a month before staining.

The axis cylinder was stained with SETO's modification of BIELSCHOWSKY's silver impregnation. The myelin sheath was stained with EHRLICH's acid hematoxyline method.

III. THE NEUROPATHOLOGICAL CHANGES IN THE DILATED PORTION OF THE CONGENITAL MEGACOLON

The wall of the dilated portion was generally thickened. Many nerve fibers were found in AUERBACH's plexus between markedly thickened muscular layers. The number of ganglion cells in AUERBACH's plexus of this case was much less than in the normal colon. Among these ganglion cells, morbid cells were observed. Many processes of the ganglion cell were seen. Some with a bundle came out of the cell body forming the so-called "Fortsatzdisharmonie" (STÖHR). (Fig. 1.)

The nucleus was found sometimes in the margin of the cell body, which gave an appearance of so-called "Kern-Randstellung" or "exzentrischer Nucleus" (FEYRTER). (Fig. 2.)

Abnormal swellings like spindles or beads were found here and there in the course of sensory nerves in the muscular layers. (Fig. 3.)

These abnormal swellings of the nerves were also found in the thick nerves in the submucous layer and in the lamina muscularis mucosae. (Fig. 4, 5.) In the lamina propria mucosae, these abnormal swellings of sensory nerves often contained vacuoles. (Fig. 6.) The staining of the axis cylinder in the areas of swelling appeared dim. By their thickness, they could be easily distinguished from thin autonomic nerve fibers. Except in the swollen parts, these fibers showed the normal thickness of sensory nerve fibers. The lack of SCHWANN's nuclei enabled them to be easily differentiated from "the distal nervous syncitium" (JABONERO) or "praeterminalreticula" (STÖHR). A normal sensory nerve fiber has many varicosities in its course, but it does not show sporadic swellings like beads, spindles, ampules or sausages. They show neither dim staining nor vacuoles.

The auther found abnormally developed "praeterminalreticula" and "terminalreticula" of autonomic nerves in the submucous layer and the mucous layer. (Fig. 7,8.)

These reticula formed abnormal wide bands occasionally spreading like veils and they consisted of thick fibrils with large particles at their knots. Around the blood vessels in the submucous layer, many strands of "terminalreticula" were interwoven. And in their strands of meshwork, the ramified neurofibrils were thick. (Fig.8.)

On the other hand many thin fibers of autonomic nerves, without making "terminalreticulum", spread in the mucous membrane. Sometimes these thin nerve fibers run, in bundles, into the lamina propria mucosae and extended between the crypts of the intestine. As stated above, "terminalreticula" in the dilated portion of megacolon were generally in a highly stimulated condition. Besides the above mentioned abnormal finding, normal sensory nerves and their endings were also observed.

In this case, myelin sheath staining of the nerves in the dilated portion showed much fewer numbers of medium sized (over 3μ in diameter) myelinated fibers than in a normal descending colon. Various sized myelinated nerve fibers in the submucous and mucous layers existed in this case in the following ratio; large sized : medium sized : small sized 1 : 9 : 39. Among them there were found granular degeneration.

IV. Discussion

By the silver staining, the abnormally deformed thick nerve fibers in the dilated portion of this megacolon were considered degenerated sensory nerve fibers, because they gave the same morphological aspect as the degeneration of sensory fibers following posterior rhizotomy. On myelin sheath staining, the myelin sheaths of the nerves showed also a granular degeneration. These changes of the myelin sheaths confirm the degeneration of abnormally deformed nerve fibers observed in silver staining. Following posterior rhizotomy, OTSU found, in AUERBACH's plexus and in the muscular layer of a dog's pylorus, the same deformed sensory nerve fibers, but he could not determine whether they were degenerated nerve fibers or not. From the author's findings, the author believes, they were surely degenerated fibers. The

same opinion is reported by SPIELMEYER. Recently HAFERKAMP found in the submucous layer of the rectum of a case of proctitis, ampule-like deformed nerve fibers, of which he reported to be degenerated nerve fibers due to acute inflammation. The author found such deformed nerves in the ascending colon of a case of CROHN's disease. These abnormally deformed sensory nerves may be caused by inflammation, mechanical, or chemical stimuli from retained contents. Degeneration of nerve fibers in these cases may begin in the peripheral regions. In the dilated portion of the megacolon, normal unforked or forked endings were found as well, but tangled sensory nerve endings, which was found by OTSU, were not observed.

Medium sized myelinated nerves are much fewer in the dilated portion of the megacolon than in the normal descending colon. This finding may be due to degeneration and disappearance of medium sized myelinated nerves in the course of chronic stimulation. Considering the medium sized myelinated nerves as sensory in nature, the decreased number of them in the dilated portion of the megacolon may agree with the physiological findings that the dilated portion has poor sensitivity.

UEDA found in AUEREACH's plexus of the dilated portion of the congenital megacolon a decreased number of ganglion cells, which has been also confirmed in the author's observations. The author found a morbid degeneration of ganglion cells described as "Fortsatzdisharmonie" by STÖHR and "Kern-Randstellung" or "exzentrischer Nucleus" by FEYRTER. Since ganglion cells in AUERBACH's plexus consist of parasympathetic nerve cells, a decrease in number or degeneration of these nerve cells causes a disturbance in the parasympathetic innervation of the dilated portion.

On the contrary, the author found an abnormally proliferated autonomic "praeterminalreticula" and "terminalreticula" in the peripheral layers of the dilated portion which show a continuous stimulation of sympathetic nerves. The ganglion cells in AUERBACH's plexus, which belong to the parasympathetic, are in regression. Therefore, the proliferation of reticular formations of autonomic nerves must be regarded as the stimulated state of sympathetic nerves. Thus the dilated portion of the megacolon is under much stronger innervation of sympathetic nerves than the normal portions of the colon. STÖHR reported on the degeneration of "terminalreticula" in the peripheral layers of the megacolon. In the dilated portion of this case, such a degenerative picture of "terminalreticula" was not observed.

As to the etiology of megacolon many authors feel it is due to mechanical cause, congenital anomaly, or a nervous factor, the last of which is insisted upon by PENNATO, FENWICK, ROYLE and RETYLOFF, and it seems to be a most popular theory. TAKAYASU pointed out the organic changes of autonomic innervation in the megacolon. ISHIKAWA and SEKIGAWA specially maintained megacolon is due to disturbances of the parasympathetic innervation. A. W. FISCHER, OTSUKI and ISHIYAMA reported treatment of megacolon by sympathectomy. In 1948 WHITEHOUSE and KERNOHAN reported that was a marked decrease in number of nerve cells of AUEREACH's plexus and even disappearance of the nerve cells in the strictured portion of the megacolon resu-

Fig. 1. Abnormally deformed ganglion cell in Auerbach's plexus of the dilated portion of a congenital megacolon (so-called "Fortsatz-disharmonie") B-S. × 600

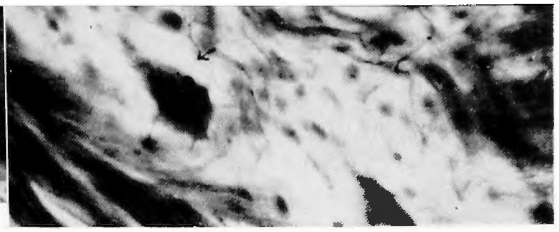

Fig. 2. Abnormally deformed ganglion cells in Auerbach's plexus of the dilated portion of a congenital megacolon (so-called "Kern-Randstellung") B-S. × 300

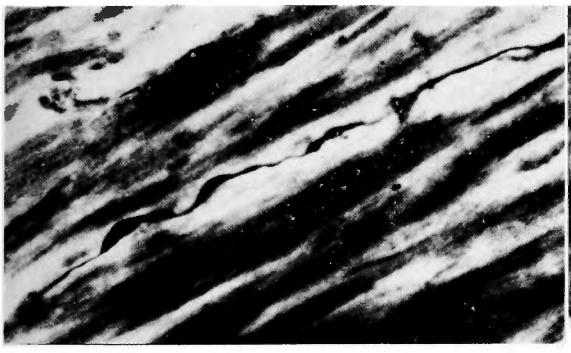

Fig. 3. Abnormally deformed sensory nerve fiber in the muscular layer of the dilated portion of a congenital megacolon B-S. × 600

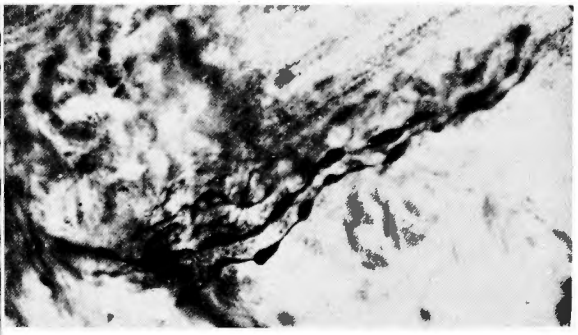

Fig. 4. Abnormally deformed sensory nerve fibers in the submucous layer of the dilated portion of a congenital megacolon B-S. × 600

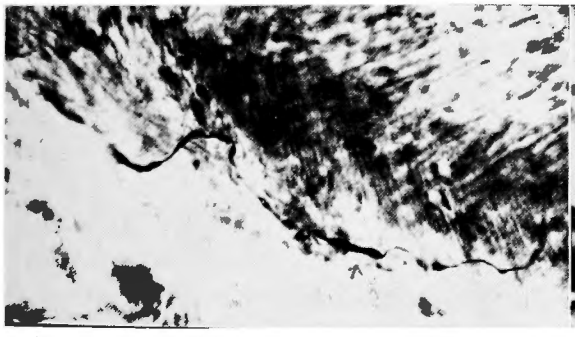

Fig. 5. Abnormally deformed sensory nerve fiber in the tunica muscularis mucosae of the dilated portion of a congenital megacolon B-S. × 400

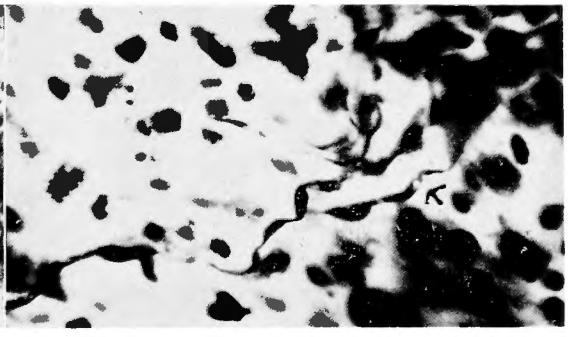

Fig. 6. Abnormally deformed sensory nerve endings in the mucous membrane of the dilated portion of a congenital megacolon B-S. × 800

Fig. 7. Abnormally proliferated "autonomic terminalreticulum" in the mucous membrane of the dilated portion of a congenital megacolon B-S. × 1000

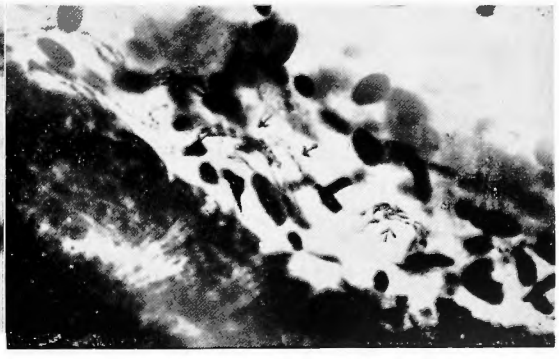

Fig. 8. Abnormally proliferated "autonomic terminalreticula" around the blood vessel in the submucous layer of the dilated portion of a congenital megacolon B-S. × 600

lting in disturbance of passive the intestinal contents and this causing a compensatory dilatation of the proximal portions. However, if disturbance in passage at the stricture is the only cause, as maintained by WHITEHOUSE, it would cause general symptoms of the ileus rather than showing a localized dilatation of the colon. Recently UEDA pointed out a decrease in the number of the ganglion cells in AUEREACH'S plexus in the dilated portion. So, he maintains that, besides the strictured portion, the neurohistological changes in the dilated portion of megaclon also play a role in its pathogenesis. The author also observed a decreased number of the ganglion cells and found a morbid regression of the ganglion cells also. A marked proliferation of "praeterminalreticulum" and "terminalreticulum" which are considered as a part of the sympathetic system were found in the peripheral layers in the dilated portoin. These facts suggest a decreased parasympathetic and a stimulated sympathetic control, resulting in hypotonia of the intestinal wall, a decreased and inhibited peristalsis of the colon, increased absorption and finally an impaired passage of intestinal contents, leading to a hard stool and chronic obstipation. The degeneration and the decrease in the number of the sensory nerves may cause hyposensitivity, unsusceptibility to accumulated contents, and stagnation of contents in the dilated portion due to the lack of defecatory reflex. The visceral sensitivity is poor in the dilated portion of the megacolon. Most of megacolons develop in the distal portion of the colon, where the sacral sensory innervation is dominant. The decreased response to a defecatory stimulus is due to a degeneration or partial diminution of these sacral sensory nerves.

The author considers that these pathologic changes in the sensory nerves and the autonomic nervous system play a role as a part of pathogeneses or as supplementary factors in the development of congenital megacolon. However, the author is not sure whether they represent the etiologic factors of the disease or only the results of chronic stimulations by obstipation.

V. SUMMARY

Specimens of the dilated portion of a congenital megacolon are stained by SETO's modification of BIELSCHOWSKY's silver impregnation and EHRLICH's acid hematoxyline method with the following results:

1) The author found abnormal sensory nerves and their endings. They were swollen into ampule shapes and sometimes contained vacuoles.

2) A marked decrease in the number of medium and large sized myelinated nerves was observed in all layers of the dilated portion.

3) A decreased number of ganglion cells was observed in AUERBACH's plexus, and abnormally deformed ganglion cells also were found there.

4) The mucous membrane and submucous layer of the dilated portion had markedly proliferated "autonomic terminalreticula".

5) The above mentioned findings suggest a decreased parasympathetic and a stimulated sympathetic innervation in the dilated portion of the megacolon, resulting in a hypotonic intestinal wall, a decreased and inhibited peristalsis, increased abso-

rption, and finally an impaired passage of the intestinal contents. The degeneration or the decrease in the number of the sensrory nerves may cause hyposensitivity and stagnation of intestinal contents in the dilated portion, due to the lack of defecatory reflex.

All these neural conditions may form a constitution of obstipation. However, the author cannot determine these neural conditions as primary factors in the pathogenesis of congenital megacolon.

I am much indebted to Assistant Prof. Dr. CHUJI KIMURA of our clinic for his constant help throughout my study.

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先天性巨大結腸症の膨大部に於ける神経病理学的変化について (和文抄録)

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Bielschowsky 氏神経鍍銀法の瀬戸氏変法及び Ehrlich 氏神経髄鞘染色法を用いて先天性巨大結腸症の膨大部の標本を染色し，次の結果を得た．

1) 先天性巨大結腸症の膨大部腸壁の筋層，粘膜下層及び粘膜層内に，変性によつて所々瓶状，紡錘状又はソーセージ状に膨化し，時にはその部に空泡を有する異常形の知覚神経線維並にその終末が発見された．

2) 膨大部腸壁の全層に渡つて中径，大径の有髄神経線維の著明な減少並に変性像が認められた．

3) 膨大部腸壁の Auerbach 氏神経叢に神経節細胞の著明な減少が認められ，尚病的な異常形の神経節細胞も発見された．

4) 膨大部腸壁の粘膜層，粘膜下層に異状に発達した自律神経終末網が発見された．

5) 以上の所見は先天性巨大結腸症の膨大部に於ける副交感神経支配が減弱し交感神経支配が刺戟状態にあることを示すもので，両々相俟つて該部腸壁の緊張度の低下，蠕動運動の抑制，吸収作用の促進等を来し，そのために腸内容の移送が不充分となり，又膨大部に於ける知覚神経の変性と減少によつて該部に於ける知覚鈍麻を来し，引いては排便反射の欠如となり膨大部に腸内容が停滞するようになる．更にまた之等種々の異常神経状態が一緒になつて便秘の素質を形成するものと考察されるが，而もなお之等の異常神経状態を以て先天性巨大結腸症の成因の本態と決定することはつゝしまなければならない．